

## Mini Review

# Cancer in the Male to Female Transgender Community

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The management of cancer in male to female transgender patients (MTF) is like a three legged stool. The three legs are access, education and monitoring. Like the legs of a three legged stool, if any one of the components is missing, the stability of care is compromised.

When a person's gender identity does not match his or her physical phenotype, that person is referred to as transgender. This condition was previously referred to as gender identity disorder. However, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, now labels this constellation of findings as gender dysphoria [1].

Gender affirmation treatment includes four types of interventions: 1) changes in social expression of gender to achieve consistency with gender identity, 2) therapy with cross-sex hormones to achieve desired masculinization or feminization, 3) surgical change of genitalia and/or other sex characteristics, and 4) psychotherapy to further explore gender identity, improve body image and promote resilience [2]. It is estimated that 1.4 million persons (0.6% of U.S. adults) identify themselves as transgender as of 2016 [3,4].

Access to healthcare has been and continues to be an issue for the transgender population. The 2015 U.S. Transgender Survey (USTS) found that 25% of transgender individuals were denied health insurance coverage for gender transition care or routine care because of their reported transgender status [5]. In addition, Healthy People 2000 indicated that HIV, sexually transmitted infections (STI), psychiatric disorders, victimization and suicide prevalence rates are significantly higher among transgender individuals than heterosexuals and other LGBTQ groups [6].

Many transgender patients are dissatisfied with the care they receive [7]. Moreover, Roberts and Frantz concluded in their review that many medical practitioners are not adequately trained to deliver the health care services required by transgender patients [8], and Shires and Jaffee [7] reported that 50% of the 6,450 respondents expressed dissatisfaction with the care they received. Even among transgender patients with health insurance, discrimination in a health care setting was reported in 38% of responders [9,10]. In addition, a recent survey of transgender people found that 51% of transwomen found they had "to teach their providers about transgender people [11]".

Discrimination against transgender patients in the health care arenas continues to occur. In a landmark decision on June

15, 2020, the Supreme Court ruled that the Civil Rights Act protects gay and transgender workers from discrimination by their employers. Days later, Trump administration officials at the Department of Health and Human Services (HHS) finalized a more permissive standard for discrimination in health care. A new HHS rule will take effect in August that allows health care providers and insurers to turn away transgender patients, whether they need a routine medical check-up or care related to gender reassignment [12].

Education of both patients and physicians continues to be an issue in cancer care of transgender women. Many patients and some physicians are not aware that the prostate is not removed during sex reassignment surgery. In addition, in some patients, an orchiectomy is not performed and in others, after penectomy, the penile skin is utilized to create a neovagina. All of these circumstances have implications for cancer care in these patients. We will review the specific issues of prostate cancer, testicular cancer and penile skin and how they relate to the evaluation of this population group.

## PROSTATE CANCER

There have been eleven cases of prostate cancer reported in male to female transgender patients [4,13,14]. Of these, five started hormone therapy at the age of 45 or older when a prostate cancer may have already been present. Their age at diagnosis ranged from 54 to 78 years and PSA levels ranged from 3.3 ng/dl to 240 ng/dl. Seven had evidence of metastatic disease at the time of diagnosis. Two patients were diagnosed on the basis of an abnormal digital rectal exam (DRE), one patient was diagnosed due to an elevated PSA, one patient was diagnosed as part of an evaluation of unexplained weight loss and six patients were diagnosed during evaluations for hematuria or lower urinary tract symptoms (LUTS) and in one patient the presenting symptom was not recorded.

One likely explanation for the development of prostate cancer in these patients is that it was already present before they underwent orchiectomy or started estrogen therapy. Another explanation that has been proposed is that estrogens themselves may have promoted prostate cancer. Sharif et al. [15], performed immunohistochemical (IHC) localization in their MTF patient and demonstrated staining in the estrogen receptor alpha

and progesterone receptor in malignant glands which raised concerns of the possible contributing role of exogenous estrogen therapy in tumorigenesis [15]. Similar findings in the LNCaP cell line has been reported by King et al. [16], Additional basic science support for the possible role of estrogens in an animal model has been provided by Bosland et al [17].

There are no specific guidelines as to how to screen and follow transgender female patients for prostate cancer. Gooren and Morgentaler [18], have proposed a PSA of 1 ng/dl as a normal cutoff in this population, but this was an arbitrary recommendation that has not been validated. At the present time, the best strategy would appear to be that transgender females should be screened for prostate cancer as would be done for cisgender males at a similar age with a low threshold to pursue any suspicious physical or laboratory findings.

## TESTICULAR CANCER

Testicular cancer in male to female transgender patients is rare and only three case reports have been reported in the literature [19-21]. There is no convincing evidence that testicular cancer is mediated by exogenous estrogen. What should be recognized is that male to female transgender patients who transition without undergoing a bilateral orchiectomy should be followed in the same manner as any cisgender male. A testicular exam should be part of any routine health check and if a testicular mass is palpated, then a scrotal ultrasound, testicular tumor markers and appropriate imaging studies should be performed.

## PENILE CANCER

One of the risk factors for squamous cell carcinoma of the penis is human papillomavirus (HPV) infection [22] Among the 40 types of HPV, at least 13 re considered high risk with respect to their carcinogenic potential [23] HPV related infections are more common in the transgender population [24] and therefore they are at greater risk for HPV related cancers [25].

Transgender women who have not undergone a penectomy as part of their transition or those who have undergone a penectomy with utilization of the penile skin to construct a neovagina should be screened for squamous cell cancers.

## SUMMARY

The male to female transgender population presents unique challenges to the caregiver. These patients should be treated with dignity and respect. Education of both the transgender patients and the physicians who care for them is necessary to optimize their care.

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